

PRELIMINARY AMENDMENT

Serial Number: Unknown (Cont. of Serial No. 08/389,712)

Filing Date: Unknown

Title: THERAPEUTIC INHIBITOR OF VASCULAR SMOOTH MUSCLE CELLS

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At page 59, line 13, after "(shown at #2," delete "FIGURE 1" and insert therefor --FIGURE 1B--.

At page 59, line 14, after "(#1," delete "FIGURE 1" and insert therefor --FIGURE 1B--.

**In the Claims**

Please cancel claims 1-25 without prejudice.

Please add the following new claims:

26. A method for treating a traumatized mammalian vessel, comprising, following the surgical excision or isolation of a graft vessel, exposing the graft vessel to a therapeutic agent in an amount effective to decrease or prevent diminution in the luminal area of the graft vessel following engraftment of the graft vessel.

27. The method of claim 26 wherein the exposure to the therapeutic agent is via infusion of the vessel.

28. The method of claim 27 wherein the infusion is accomplished by pressure infusion at from about 0.2 to 1 atmospheres for a time period of about 2-4 minutes.

29. The method of claim 26 wherein the therapeutic agent comprises a cytoskeletal inhibitor.

30. The method of claim 26 wherein the therapeutic agent comprises a cytochalasin or an analog thereof.

31. The method of claim 26 wherein the amount of the therapeutic agent administered is sufficient to inhibit stenosis or restenosis of the traumatized vessel.

32. A method for maintaining vessel luminal area, comprising inserting into a mammalian vessel an intravascular stent comprising an amount of a cytoskeletal inhibitor effective to reduce stenosis or restenosis upon placement of the stent.

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8 ~~33~~. The method of claim ~~32~~ wherein the intravascular stent comprises metal or plastic.

9 ~~34~~. The method of claim ~~32~~ wherein the intravascular stent comprises a biodegradable material.

10 ~~35~~. The method of claim ~~34~~ wherein the intravascular stent consists essentially of a biodegradable material.

11 ~~36~~. The method of claim ~~32~~ wherein the cytoskeletal inhibitor is in sustained release form.

12 ~~37~~. The method of claim ~~36~~ wherein the cytoskeletal inhibitor comprises a cytochalasin or an analog thereof.

13 ~~38~~. The method of claim ~~36~~ wherein the sustained release cytoskeletal inhibitor comprises a binding peptide or protein capable of specifically binding to smooth muscle cells, stromal cells or interstitial matrix surrounding smooth muscle cells.

14 ~~39~~. The method of claim ~~32~~ wherein the intravascular stent comprises a biodegradable coating or a porous non-biodegradable coating comprising the cytoskeletal inhibitor.

15 ~~40~~. The method of claim ~~32~~ wherein the cytoskeletal inhibitor comprises a cytochalasin or an analog thereof.

16 ~~41~~. The method of claim ~~32~~ wherein the vessel is subjected to further vascular trauma.

17 ~~42~~. The method of claim ~~32~~ wherein the vessel is subjected to angioplasty.

18 ~~43~~. A method for providing an intravascular stent effective to maintain vessel luminal area in a mammal, comprising coating the intravascular stent with a coating comprising a sustained

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release dosage form which comprises an amount of a cytoskeletal inhibitor effective to reduce or inhibit stenosis or restenosis of said vessel.

<sup>19</sup>  
~~44~~. The method of claim ~~43~~<sup>18</sup> wherein the stent comprises a biodegradable material.

<sup>20</sup>  
~~45~~. The method of claim ~~43~~<sup>18</sup> wherein the stent comprises plastic or metal.

<sup>21</sup>  
~~46~~. The method of claim ~~44~~<sup>19</sup> or ~~45~~<sup>20</sup> wherein the stent further comprises a therapeutic agent which is an inhibitor of smooth muscle cell proliferation.

<sup>22</sup>  
~~47~~. The method of claim ~~44~~<sup>19</sup> or ~~45~~<sup>20</sup> wherein the stent further comprises a therapeutic agent which is a cytoskeletal inhibitor.

<sup>23</sup>  
~~48~~. The method of claim ~~47~~<sup>22</sup> wherein the cytoskeletal inhibitor comprises a cytochalasin or an analog thereof.

<sup>24</sup>  
~~49~~. The method of claim ~~43~~<sup>18</sup> wherein the coating is biodegradable.

<sup>25</sup>  
~~50~~. The method of claim ~~43~~<sup>18</sup> wherein the coating is porous.

<sup>26</sup>  
~~51~~. The method of claim ~~43~~<sup>18</sup> wherein the cytoskeletal inhibitor comprises a cytochalasin or an analog thereof.

<sup>27</sup>  
~~52~~. A method for providing an intravascular stent effective to maintain vessel luminal area in a mammal, comprising introducing into the matrix of the intravascular stent an amount of a cytoskeletal inhibitor effective to reduce or inhibit stenosis or restenosis of said vessel.

<sup>28</sup>  
~~53~~. The method of claim ~~52~~<sup>27</sup> wherein the stent comprises a biodegradable material.

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<sup>27</sup>  
2954. The method of claim ~~52~~ wherein the stent comprises plastic or metal.

<sup>27</sup>  
3055. The method of claim ~~52~~ wherein the stent further comprises a coating comprising a sustained release dosage form which comprises a cytoskeletal inhibitor.

<sup>27 30</sup>  
3156. The method of claim ~~55~~ wherein the cytoskeletal inhibitor comprises a cytochalasin or an analog thereof.

<sup>32</sup>  
3257. The method of claim ~~55~~ wherein the coating is biodegradable.

<sup>33</sup>  
3358. The method of claim ~~55~~ wherein the coating is porous.

<sup>34</sup>  
3459. The method of claim ~~52~~ wherein the cytoskeletal inhibitor comprises a cytochalasin or an analog thereof.

<sup>35</sup>  
60. A method for preparing an intravascular stent effective to maintain vessel luminal area in a mammal, comprising introducing into the matrix of the intravascular stent an amount of a cytostatic therapeutic agent which does not exhibit substantial cytotoxicity, which agent is effective to reduce or inhibit stenosis or restenosis of said vessel, wherein the therapeutic agent is not heparin or a radioisotope.

<sup>35</sup>  
3661. The method of claim ~~60~~ wherein the stent comprises a biodegradable material.

<sup>35</sup>  
3772. The method of claim ~~60~~ wherein the stent comprises plastic or metal.

<sup>35</sup>  
3863. The method of claim ~~60~~ wherein the stent further comprises a coating comprising a sustained release dosage form which comprises a cytoskeletal inhibitor.

<sup>38</sup>  
3964. The method of claim ~~63~~ wherein the cytoskeletal inhibitor comprises a cytochalasin or an

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analog thereof.

40  
65. The method of claim <sup>38</sup>~~63~~ wherein the coating is biodegradable.

41  
66. The method of claim <sup>38</sup>~~63~~ wherein the coating is porous.

42  
67. The method of claim <sup>5 12 15 13 26 31 34 39</sup>~~30, 37, 40, 48, 51, 56, 59 or 64~~ wherein the cytochalasin is cytochalasin B or an analog thereof.

43  
68. The method of claim <sup>38</sup>~~63~~ wherein the sustained release form of the cytoskeletal inhibitor comprises a binding peptide or protein which specifically binds to smooth muscle cells, stromal cells, or interstitial matrix surrounding smooth muscle cells.

44  
69. The method of claim <sup>1</sup>~~26~~ wherein the therapeutic agent comprises a cytostatic agent.

45  
70. A method for maintaining vessel luminal area, comprising inserting into a mammalian vessel an intravascular stent comprising an amount of a cytochalasin or an analog thereof effective to inhibit or reduce stenosis or restenosis upon placement of the stent.

46  
71. The method of claim <sup>45</sup>~~70~~ wherein the cytochalasin or analog thereof is in sustained release form.

47  
72. The method of claim <sup>45</sup>~~70~~ wherein the matrix of the stent is impregnated with the cytochalasin or analog thereof.

48  
73. The method of claim <sup>47</sup>~~72~~ wherein the intravascular stent further comprises a coating comprising a cytostatic amount of an inhibitor of smooth muscle cell proliferation.

49  
74. The method of claim <sup>45</sup>~~70~~ wherein the intravascular stent comprises a coating comprising

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the cytochalasin or analog thereof.

<sup>50</sup>  
~~75~~. The method of claim <sup>49</sup>~~74~~ wherein the matrix is impregnated with a cytostatic amount of an inhibitor of smooth muscle cell proliferation.

<sup>51</sup>  
~~76~~. The method of claim <sup>45 46 47 49</sup>~~70, 71, 72, or 74~~ wherein the cytochalasin comprises cytochalasin B.

<sup>52</sup>  
~~77~~. A method for maintaining vessel luminal area, comprising inserting into a mammalian vessel an intravascular stent which comprises a matrix and a coating on said matrix, wherein the coating and the matrix together comprise an amount of a cytoskeletal inhibitor effective to inhibit stenosis or reduce restenosis upon placement of the therapeutic stent.

<sup>53</sup>  
~~78~~. The method of claim <sup>53</sup>~~77~~ wherein the cytoskeletal inhibitor is in sustained release form.

<sup>54</sup>  
~~79~~. The method of claim <sup>52</sup>~~77~~ wherein the cytoskeletal inhibitor comprises a cytochalasin or an analog thereof.

<sup>55</sup>  
~~80~~. The method of claim <sup>54</sup>~~79~~ wherein the cytochalasin comprises cytochalasin B.

<sup>56</sup>  
~~81~~. The method of claim <sup>46 53</sup>~~74 or 78~~ wherein the sustained release form comprises a binding peptide or protein capable of specifically binding to smooth muscle cells, stromal cells or interstitial matrix surrounding smooth muscle cells.

<sup>57</sup>  
~~82~~. The method of claim <sup>48 49 52</sup>~~73, 74 or 77~~ wherein the coating is formed from a biodegradable material.

<sup>58</sup>  
~~83~~. The method of claim <sup>45 52</sup>~~70 or 77~~ wherein the vessel is subjected to angioplasty prior to stent placement.

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59/ 84. A method for preparing a therapeutic intravascular stent effective to maintain vessel luminal area in a mammal, said method comprising treating the intravascular stent with an amount of cytochalasin or an analog thereof so as to result in the therapeutic stent.

60/ 85. The method of claim 84 <sup>59</sup> wherein the cytochalasin or analog thereof is introduced into the matrix of the stent.

61/ 86. The method of claim 85 <sup>60</sup> wherein the stent further comprises a coating comprising a cytostatic amount of an inhibitor of smooth muscle cell proliferation.

62/ 87. The method of claim 84 <sup>59</sup> wherein the stent is coated with a coating comprising cytochalasin or analog thereof.

63/ 88. The method of claim 87 <sup>62</sup> wherein the stent matrix comprises a cytostatic amount of an inhibitor of smooth muscle cell proliferation.

64/ 89. The method of claim 84, 85, or 87 <sup>59, 60, 62</sup> wherein the cytochalasin or an analog thereof is in sustained release dosage form.

65/ 90. The method of claim 84, 85, or 87 <sup>59, 60, 62</sup> wherein the cytochalasin comprises cytochalasin B.

66/ 91. A method for preparing a coated therapeutic intravascular stent, which comprises a matrix and a coating on said matrix, effective to maintain vessel luminal area in a mammal, said method comprising introducing to the coating and the matrix of the intravascular stent an amount of a cytoskeletal inhibitor so as to result in the therapeutic stent.

67/ 92. The method of claim 91 <sup>66</sup> wherein the cytoskeletal inhibitor is a cytochalasin or an analog thereof.

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68  
93. The method of claim ~~91~~<sup>66</sup> wherein the cytoskeletal inhibitor in the coating is in sustained release dosage form.

89  
94. The method of claim ~~91~~<sup>66</sup> wherein the cytoskeletal inhibitor in the matrix is in sustained release dosage form.

79  
95. The method of claim ~~86, 87, 88~~<sup>61 62 63 66</sup> or ~~91~~<sup>66</sup> wherein the coating is formed from a biodegradable material.

71  
96. The method of claim ~~84~~<sup>51 66</sup> or ~~91~~<sup>66</sup> wherein the intravascular stent comprises plastic or metal.

72  
97. The method of claim ~~84~~<sup>51 66</sup> or ~~91~~<sup>66</sup> wherein the intravascular stent comprises a biodegradable material.

73  
98. A method for maintaining vessel luminal area, comprising administering to a mammal an amount of a cytoskeletal inhibitor effective to biologically stent said vessel, wherein the cytoskeletal inhibitor is administered in conjunction with intravascular stent placement.

74  
99. The method of claim ~~98~~<sup>73</sup> wherein the intravascular stent comprises an amount of a cytoskeletal inhibitor effective to inhibit stenosis or reduce restenosis following stent placement.

75  
100. The method of claim ~~99~~<sup>74</sup> wherein the intravascular stent comprises an amount of cytoskeletal inhibitor effective to inhibit vascular smooth muscle cell proliferation.

Remarks

Claims 1-25 having been canceled, and claims 26-100 having been added, the claims now pending are claims 26-100.

The amendment to the specification at page 1, line 6, is to indicate the relationship